

IN THE CLAIMS:

For the convenience of the Examiner, all claims being examined, whether or not amended, are presented below.

1. **(Previously presented)** A cell containing
 - (a) a first genetic construct or pair of first genetic constructs encoding chimeric proteins comprising (i) at least one ligand-binding domain which can bind a selected ligand and (ii) a second protein domain, which is heterologous with respect to at least one of the ligand-binding domains, and
 - (b) a target gene encoding an angiogenesis inhibitor under the expression control of a transcriptional control element responsive to binding of ligand to the ligand binding domain, wherein said angiogenesis inhibitor is angiostatin, and wherein transcription of the target gene is regulated in a manner dependent on the expression of the chimeric protein and the presence of the ligand.
2. **(Original)** The cell of claim 1 wherein the chimeric proteins multimerize upon addition of ligand and wherein transcription of the target gene is responsive to the multimerization of the chimeric proteins.
3. **(Original)** The cell of claim 1 wherein the ligand binding domain is selected from the group consisting of an immunophilin domain, a cyclophilin domain, a steroid hormone binding domain and an antibiotic binding domain.
4. **(Cancelled)**
5. **(Currently amended)** The ~~engineered~~ cell of claim 1 in which the target gene encodes a peptide sequence of human origin.
6. **(Withdrawn)** A cell containing

- (a) a first DNA construct or pair of first DNA constructs encoding chimeric proteins comprising (i) at least one receptor domain capable of binding to a selected ligand and (ii) another protein domain, heterologous with respect to the receptor domain, and
- (b) a target gene encoding a tumor specific antigen under the expression control of a transcriptional control element responsive to binding of ligand to the ligand binding domain.

7. **(Withdrawn)** The cell of claim 6 wherein the chimeric proteins multimerize upon addition of ligand and wherein transcription of the target gene is responsive to the multimerization of the chimeric proteins.
8. **(Withdrawn)** The cell of claim 6 wherein the ligand binding domain is selected from the group consisting of an immunophilin domain, a cyclophilin domain, a steroid hormone binding domain and an antibiotic binding domain.
9. **(Withdrawn)** A cell containing
 - (a) a DNA construct encoding a chimeric protein consisting essentially of (i) a receptor domain capable of binding to a selected ligand, (ii) a transcription activation domain, heterologous with respect to the receptor domain, (iii) and a DNA binding domain; and
 - (b) a target gene encoding beta-interferon or a cytokine under the expression control of a transcriptional control element responsive to binding of ligand to the ligand binding domain.
10. **(Withdrawn)** The cell of claim 9 wherein the ligand binding domain is selected from the group consisting of a steroid hormone binding domain and an antibiotic binding domain.
11. **(Withdrawn)** The cell of claim 6 or 9 in which the target gene encodes a peptide sequence of human origin.
12. **(Withdrawn)** A recombinant virus containing

- (a) a first DNA construct or pair of first DNA constructs encoding chimeric proteins comprising (i) at least one receptor domain capable of binding to a selected ligand and (ii) another protein domain, heterologous with respect to the receptor domain, and
- (b) a target gene encoding an angiogenesis inhibitor, a tumor specific antigen, a cytokine or beta-interferon under the expression control of a transcriptional control element responsive to binding of ligand to the ligand binding domain.

13. **(Withdrawn)** The recombinant virus of claim 12 wherein the virus is selected from the group consisting of adenovirus, adeno-associated virus, retrovirus and herpesvirus.

14. **(Previously presented)** A method for rendering a cell capable of regulatable expression of a target gene following exposure of said cell to a selected ligand, which method comprises introducing into said cell:

- (a) a first genetic construct or pair of first genetic constructs encoding chimeric proteins comprising (i) at least one ligand-binding domain which can bind a selected ligand and (ii) a second protein domain, which is heterologous with respect to at least one of the ligand-binding domains, and
- (b) a target gene under the expression control of a transcriptional control element responsive to binding of ligand to the ligand binding domain,

wherein the target gene encodes an angiogenesis inhibitor, which angiogenesis inhibitor is angiostatin, and wherein the transcription of the target gene is regulated in a manner dependent on the expression of the chimeric protein and the presence of the ligand.

15 **(Cancelled)**

16 **(Withdrawn)** A method for rendering cells capable of regulatable expression of a target gene following exposure of the cells to a selected ligand, which method comprises introducing into the cells:

- (a) a DNA construct encoding a chimeric protein consisting essentially of (i) a receptor domain capable of binding to a selected ligand, (ii) a transcription activation domain, heterologous with respect to the receptor domain, (iii) and a DNA binding domain; and

(b) a target gene encoding beta-interferon or a cytokine under the expression control of a transcriptional control element responsive to binding of ligand to the ligand binding domain.

17. **(Previously presented)** The method of claim 14 wherein the genetic constructs are introduced into a cell maintained in vitro.

18. **(Previously presented)** The method of claim 14 wherein the genetic constructs are introduced into a cell present within a host organism.

19. **(Original)** The method of claim 14 wherein the chimeric proteins multimerize upon addition of ligand and wherein transcription of the target gene is responsive to the multimerization of the chimeric proteins.

20. **(Previously presented)** The method of claim 14 wherein the ligand binding domain is selected from the group consisting of an immunophilin domain, a cyclophilin domain, a steroid hormone binding domain and an antibiotic binding domain.

21. **(Withdrawn)** A method for treating cancer in a mammalian host organism containing cells which:

contain (a) a first DNA construct or pair of first DNA constructs encoding chimeric proteins comprising (i) at least one receptor domain capable of binding to a selected ligand and (ii) another protein domain, heterologous with respect to the receptor domain, and

(b) a target gene under the expression control of a transcriptional control element responsive to binding of ligand to the ligand binding domain; and

which express the target gene, following exposure to the selected ligand;

wherein the target gene encodes an angiogenesis inhibitor, a tumor-specific antigen or a cytokine;

which method comprises administering to said mammalian host an effective amount of a selected ligand capable of binding to the chimeric protein to effect observable expression of the target gene.

22. **(Withdrawn)** A method for treating MS episodes in a mammalian host organism containing cells which:

contain (a) a first DNA construct or pair of first DNA constructs encoding chimeric proteins comprising (i) at least one receptor domain capable of binding to a selected ligand and (ii) another protein domain, heterologous with respect to the receptor domain, and
(b) a target gene encoding beta-interferon under the expression control of a transcriptional control element responsive to binding of ligand to the ligand binding domain; and

which express the target gene, following exposure to the selected ligand;
which method comprises administering to said mammalian host an effective amount of a selected ligand capable of binding to the chimeric protein to effect observable expression of the target beta-interferon gene.

23. **(Withdrawn)** A method for treating HIV infection in a mammalian host organism containing cells which: contain

(a) a first DNA construct or pair of first DNA constructs encoding chimeric proteins comprising (i) at least one receptor domain capable of binding to a selected ligand and (ii) another protein domain, heterologous with respect to the receptor domain, and
(b) a target gene under the expression control of a transcriptional control element responsive to binding of ligand to the ligand binding domain; and

which express the target gene, following exposure to the selected ligand;
wherein the target gene encodes a ribozyme or antisense message directed against an HIV nucleotide sequence;
which method comprises administering to said mammalian host an effective amount of a selected ligand capable of binding to the chimeric protein to effect observable expression of the target gene.

24. **(Previously presented)** The method of claim 14, wherein at least one of (a) or (b) is introduced into said cell by a viral vector.

25. **(Previously presented)** The method of claim 24, wherein the viral vector is selected from the group consisting of adenovirus, adeno-associated virus, herpesvirus, and retrovirus.
26. **(Previously presented)** The method of claim 14, wherein the cell is a mammalian cell.
27. **(Previously presented)** The method of claim 26, wherein the mammalian cell is a human cell.
28. **(Previously presented)** The method of claim 14, wherein the cell is a cell type selected from the group consisting of neural, mesenchymal, cutaneous, mucosal, stromal, spleen, reticuloendothelial, epithelial, endothelial, kidney, gastrointestinal and pulmonary cells.
29. **(Previously presented)** The method of claim 14, wherein the genetic construct further comprises one or more selectable markers.
30. **(Previously presented)** The method of claim 29, wherein the selectable marker is selected from the group consisting of an antibiotic resistance gene and herpes simplex virus-thymidine kinase.
31. **(Previously presented)** The method of claim 14, wherein the target gene is a human gene.
32. **(Previously presented)** The method of claim 14, wherein the selected ligand binds the ligand-binding domain with a K_d value less than 10^{-6} M.
33. **(Previously presented)** The method of claim 14, wherein the selected ligand binds the ligand-binding domain with a K_d value less than 10^{-9} M.
34. **(Previously presented)** The method of claim 14, wherein the selected ligand is not a protein and wherein the selected ligand has a molecular weight less than 5 kDa.

35. **(Previously presented)** The method of claim 14, wherein the chimeric protein includes two or more ligand-binding domains having different ligand binding specificities.

36. **(Previously presented)** The method of claim 14, wherein at least one of the ligand-binding domains is from 50 to 350 amino acid residues in length.

37. **(Previously presented)** The method of claim 14, wherein said selected ligand is membrane permeable.

38. **(Previously presented)** The method of claim 14, wherein said selected ligand is orally active.